	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	1225	elisa adj kit	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 11:07			0
2	BRS	L2	19	(cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 11:09			0
3	BRS	L3	0	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 11:09			0
4	BRS	L4	0	2 same trypsin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 11:09			0

	Type	L #	Hits	Search T xt	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L5	2	(3 or 4) same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:18			0
2	BRS	L6	109191	(biological adj matrix) or cartilage or (bone adj matrix) or collagen or hyaluronan or (fibrin adj gel) or (carbon adj fiber) or (polylactic adj acid)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:22			0
3	BRS	L7	19	((biological adj matrix) or cartilage or (bone adj matrix) or collagen or hyaluronan or (fibrin adj gel) or (carbon adj fiber) or (polylactic adj acid)) same (hCOMP or (cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:23			0
4	BRS	L4	10	hCOMP	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:25			0
5	BRS	L8	0	hCOMP near protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:26			0
6	BRS	L3	20	(COMP adj protein) or (cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 09:26			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	20	(COMP adj protein) or (cartilage adj oligomeric adj matrix adj protein) or (thrombospondin-5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 10:09			0
2	BRS	L2	3	1 same (recombinant or expression)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 10:10			0
3	BRS	L3	0	2 same calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/03 10:10			0

=> d his

(FILE 'HOME' ENTERED AT 09:34:01 ON 03 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
09:35:12 ON 03 JUL 2002
L1 0 S HCOMP (A) PROTEIN
L2 871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR (THROMBOSPONDIN-5)
L3 68 S L2 (P) CALCIUM
L4 46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L5 45 S L4 NOT L3
L6 1 S L5 (P) CALCIUM
L7 21 DUPLICATE REMOVE L3 (47 DUPLICATES REMOVED)
L8 596928 S (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
L9 21 S L7 (P) L8
L10 3377 S ELISA KIT
L11 0 S L10 (P) (L2 OR L4)
L12 1 S L7 (P) TRYPSIN
L13 0 S L12 NOT L7

=> log y

```
FILE 'HOME' ENTERED AT 09:57:26 O   3 JUL 2002

=> s human cartilage oligomeric cartilage matrix protein
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.63       0.63

FILE 'MEDLINE' ENTERED AT 09:58:58 ON 03 JUL 2002

FILE 'CAPLUS' ENTERED AT 09:58:58 ON 03 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 09:58:58 ON 03 JUL 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC. (R)

FILE 'EMBASE' ENTERED AT 09:58:58 ON 03 JUL 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'SCISEARCH' ENTERED AT 09:58:58 ON 03 JUL 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 09:58:58 ON 03 JUL 2002

=> s human cartilage oligomeric matrix protein
   3 FILES SEARCHED...
L1          46 HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN

=> s l1 (p) (recombinant or express?)
L2          12 L1 (P) (RECOMBINANT OR EXPRESS?)

=> duplicate remove l2
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L2
L3            5 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)

=> d l3 1-5 ibib abs

L3   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2001:230958  CAPLUS
DOCUMENT NUMBER:         135:314320
TITLE:                   Analysis of the promoter region of human cartilage
                         oligomeric matrix protein (COMP)
AUTHOR(S):               Deere, Michelle; Hall, Catherine Rhoades; Gunning,
                         Kerry B.; LeFebvre, Veronique; Ridall, Amy L.; Hecht,
                         Jacqueline T.
CORPORATE SOURCE:        Department of Pediatrics, University of Texas Medical
                         School at Houston, Houston, TX, 77030, USA
SOURCE:                  Matrix Biology (2001), 19(8), 783-792
                         CODEN: MTBOEC; ISSN: 0945-053X
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Cartilage oligomeric matrix protein (COMP) is an extracellular matrix
     protein expressed in cartilage, ligament, and tendon.  The importance of
     COMP in the matrix of these cells is underscored by the discovery that
     mutations in COMP cause the skeletal dysplasias, pseudoachondroplasia
     (PSACH) and multiple epiphyseal dysplasia (EDM1).  Here, the authors
     present the first report on the anal. of the human COMP promoter region in
     cartilage, ligament, and tendon cells.  A 1.7-kb region of the COMP
     promoter has been cloned and sequenced and no TATA or CAAT boxes were
     found.  Primer extension identified multiple transcription start sites.
```

All four transcription start sites were utilized in chondrocytes with only three of them utilized in tendon and ligament cells. Differential regulation was obsd. for different parts of this 1.7-kb region with the 370-bp proximal region conveying the strongest promoter activity. The highest activity was obsd. in tendon and ligament. Finally, the authors provide evidence that the DNA binding protein SP1 plays a role in the regulation of COMP expression. These results indicate that COMP expression within these cells is regulated in a unique manner that differs from the expression of other extracellular matrix genes.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:535287 CAPLUS
DOCUMENT NUMBER: 133:145901
TITLE: COMP/TSP-1, COMP/TSP-2 and other chimeric proteins as angiogenesis and HIV inhibitor
INVENTOR(S): Lawler, John W.
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044908	A2	20000803	WO 2000-US2482	20000201
WO 2000044908	A3	20010215		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1149168	A2	20011031	EP 2000-910035	20000201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-118053P P 19990201
WO 2000-US2482 W 20000201

AB Tumors attract blood vessels in order to grow by a process called angiogenesis. The relative quantity of stimulators and inhibitors is an important detg. factor for the initiation of angiogenesis. Thrombospondins-1 and -2 are adhesive glycoproteins that have the ability to inhibit angiogenesis. This inhibiting activity has been mapped to the type 1 repeats of TSP-1 and TSP-2. The invention includes chimeric proteins that contain anti-angiogenic portions of TSP-1, TSP-2, endostatin, angiostatin, platelet factor 4, or prolactin, linked to a portion of the N-terminal region of ***human*** ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) that allows formation of pentamers. Also described herein are the nucleic acid mols., vectors, and host cells for ***expressing*** and producing these chimeric proteins. Further embodiments of the invention include methods to treat humans or other mammals with anti-angiogenic proteins to reduce tumor size or rate of growth. Since the type 1 repeat region of TSP-1 and TSP-2 reportedly inhibits HIV infection, chimeric proteins comprising these repeats may also be used for this purpose, as well as to inhibit angiogenesis.

L3 ANSWER 3 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000503946 MEDLINE
DOCUMENT NUMBER: 20505681 PubMed ID: 11052496
TITLE: Molecular cloning, sequencing, and tissue and developmental expression of mouse cartilage oligomeric matrix protein (COMP).
AUTHOR: Fang C; Carlson C S; Leslie M P; Tulli H; Stolerman E; Perris R; Ni L; Di Cesare P E
CORPORATE SOURCE: Musculoskeletal Research Center, Department of Orthopaedic

Surgery, New York University Medical Center-Hospital for Joint Disease, New York 10003, USA.
CONTRACT NUMBER: R01-RR14099 (NCRR)
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (2000 Jul) 18 (4) 593-603. Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AI390155; GENBANK-AI413579; GENBANK-AI426247; GENBANK-AI649107; GENBANK-AI664561; GENBANK-AI892139
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001107

AB Mouse cartilage oligomeric matrix protein cDNA was cloned and sequenced by a reverse transcription-polymerase chain reaction. The open reading frame encoded a product of 755 amino acids that shares a high degree of identity to and possesses all the characteristic molecular features of both rat and ***human*** ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** . This suggests that cartilage oligomeric matrix protein is highly conserved during evolution. The clone was 83, 84, and 95% identical to human, bovine, and rat cartilage oligomeric matrix protein cDNA, respectively. In tissues from the adult mouse, cartilage oligomeric matrix protein was ***expressed*** not only in cartilage and tendon but in trachea, bone, skeletal muscle, eye, heart, and placenta as well, and no ***expression*** was found in other tissues. Immunohistology revealed that cartilage oligomeric matrix was deposited as early as 10 days post coitus in predifferentiated mouse embryo mesenchyme. It was detected in all cartilaginous tissues and in the skeletal muscles of the embryo at day 13. As development progressed, accumulation of cartilage oligomeric matrix protein was marked in the growth plate. At 19 days post coitus, it was prominently deposited in the hypertrophic zone of the growth plate, perichondrium, and periosteum and in the superficial layer of the articular cartilage surface but was absent in the more central areas of the epiphyseal cartilage. The restricted tissue distribution and ***expression*** of cartilage oligomeric matrix protein in developing as well as adult mouse tissues suggest the regulation of this protein at the transcriptional level. The findings reported herein are the first detailed characterization of the distribution of cartilage oligomeric matrix protein during early skeletal development of the mouse.

L3 ANSWER 4 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999303228 MEDLINE
DOCUMENT NUMBER: 99303228 PubMed ID: 10376735
TITLE: Localization and expression of cartilage oligomeric matrix protein by human rheumatoid and osteoarthritic synovium and cartilage.
AUTHOR: Di Cesare P E; Fang C; Leslie M P; Della Valle C J; Gold J M; Tulli H; Perris R; Carlson C S
CORPORATE SOURCE: Musculoskeletal Research Center, Department of Orthopaedic Surgery, New York University Medical Center-Hospital for Joint Diseases, New York 10003, USA.. PEDiCesare@aol.com
CONTRACT NUMBER: RR08562 (NCRR)
SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (1999 May) 17 (3) 437-45. Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990630

AB Synovium and cartilage from patients with osteoarthritis or rheumatoid arthritis were analyzed for ***expression*** of cartilage oligomeric matrix protein. Immunostaining of synovium with antiserum to cartilage oligomeric matrix protein demonstrated positive staining in both diseases. In osteoarthritis, there was positive staining within the synovial cells and immediately subjacent connective tissue, with less intense staining in the deeper connective tissue. In rheumatoid arthritis, there was less intense staining within the synovial cells and marked intense staining in

the deeper connective tissue. In situ hybridization performed with an antisense digoxigenin-labeled riboprobe to ***human*** ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** confirmed the presence of cartilage oligomeric matrix protein mRNA in the cells of the synovial lining in both types of synovium. Quantitative polymerase chain reaction with a cartilage oligomeric matrix protein MIMIC demonstrated increased cartilage oligomeric matrix protein mRNA in rheumatoid cartilage and synovium as compared with osteoarthritic cartilage and synovium, respectively; mRNA levels in rheumatoid synovium were similar to those from osteoarthritic chondrocytes. As a result of the high ***expression*** of cartilage oligomeric matrix protein from rheumatoid synovium, inflammatory synovium should be considered as a potential tissue source of cartilage oligomeric matrix protein in any investigation of biological markers of cartilage metabolism. The upregulated ***expression*** of cartilage oligomeric matrix protein in inflammatory tissues suggests its in vivo regulation by cytokines.

L3 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:384875 BIOSIS
DOCUMENT NUMBER: PREV199900384875
TITLE: Identification of novel pro-alpha2(IX) collagen gene mutations in two families with distinctive oligo-epiphyseal forms of multiple epiphyseal dysplasia.
AUTHOR(S): Holden, Paul; Canty, Elizabeth G.; Mortier, Geert R.; Zabel, Bernhard; Spranger, Jurgen; Carr, Andrew; Grant, Michael E.; Loughlin, John A.; Briggs, Michael D. (1)
CORPORATE SOURCE: (1) Wellcome Trust Centre for Cell-Matrix Research, School of Biological Sciences, University of Manchester, Oxford Road, 2.205 Stopford Building, Manchester, M13 9PT UK
SOURCE: American Journal of Human Genetics, (July, 1999) Vol. 65, No. 1, pp. 31-38.
ISSN: 0002-9297.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Multiple epiphyseal dysplasia (MED) is a genetically heterogeneous disorder with marked clinical and radiographic variability. Traditionally, the mild "Ribbing" and severe "Fairbank" types have been used to define a broad phenotypic spectrum. Mutations in the gene encoding cartilage oligomeric-matrix protein have been shown to result in several types of MED, whereas mutations in the gene encoding the alpha2 chain of type IX collagen (COL9A2) have so far been found only in two families with the Fairbank type of MED. Type IX collagen is a heterotrimer of pro-alpha chains derived from three distinct genes-COL9A1, COL9A2, and COL9A3. In this article, we describe two families with distinctive oligo-epiphyseal forms of MED, which are heterozygous for different mutations in the COL9A2 exon 3/intron 3 splice-donor site. Both of these mutations result in the skipping of exon 3 from COL9A2 mRNA, but the position of the mutation in the splice-donor site determines the stability of the mRNA produced from the mutant COL9A2 allele.

```
=> d his

     (FILE 'HOME' ENTERED AT 09:57:26 ON 03 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:58:58 ON 03 JUL 2002
L1            46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L2            12 S L1 (P) (RECOMBINANT OR EXPRESS?)
L3             5 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)

=> s l3 (p) calcium
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L22 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L24 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26 (P) CALCIUM'
L4            0 L3 (P) CALCIUM

=> s (CARTILAGE OLIGOMERIC MATRIX PROTEIN) or thrombospondin-5
```

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   5 FILES SEARCHED...
L5          871 (CARTILAGE OLIGOME[redacted] MATRIX PROTEIN) OR THROMBOSPO[redacted]N-5

=> s l5 (p) (recombinant or express?)
L6          256 L5 (P) (RECOMBINANT OR EXPRESS?)

=> s l6 (p) calcium
L7           28 L6 (P) CALCIUM

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8             6 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 09:57:26 ON 03 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:58:58 ON 03 JUL 2002
L1             46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L2             12 S L1 (P) (RECOMBINANT OR EXPRESS?)
L3              5 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)
L4              0 S L3 (P) CALCIUM
L5            871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L6            256 S L5 (P) (RECOMBINANT OR EXPRESS?)
L7             28 S L6 (P) CALCIUM
L8              6 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)

=> s l8 not l3
L9              6 L8 NOT L3

=> d l9 1-6 ibib abs

L9   ANSWER 1 OF 6     MEDLINE
ACCESSION NUMBER:   2001196441     MEDLINE
DOCUMENT NUMBER:    21125809   PubMed ID: 11084047
TITLE:              Mutations in cartilage oligomeric matrix protein causing
                    pseudoachondroplasia and multiple epiphyseal dysplasia
                    affect binding of calcium and collagen I, II, and IX.
AUTHOR:             Thur J; Rosenberg K; Nitsche D P; Pihlajamaa T; Ala-Kokko
                    L; Heinegard D; Paulsson M; Maurer P
CORPORATE SOURCE:   Institute for Biochemistry, Medical Faculty, University of
                    Cologne, D-50931 Koln, Germany.
SOURCE:             JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Mar 2) 276 (9)
                    6083-92.
                    Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200104
ENTRY DATE:         Entered STN: 20010410
                    Last Updated on STN: 20010410
                    Entered Medline: 20010405
AB   Mutations in type 3 repeats of   ***cartilage***     ***oligomeric***
       ***matrix***     ***protein***   (COMP) cause two skeletal dysplasias,
     pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED). We
       ***expressed***     ***recombinant***   wild-type COMP that showed
     structural and functional properties identical to COMP isolated from
     cartilage. A fragment encompassing the eight type 3 repeats binds 14
       ***calcium***   ions with moderate affinity and high cooperativity and
     presumably forms one large disulfide-bonded folding unit. A
       ***recombinant***   PSACH mutant COMP in which Asp-469 was deleted (D469
     Delta) and a MED mutant COMP in which Asp-361 was substituted by Tyr
     (D361Y) were both secreted into the cell culture medium of human cells.
     Circular dichroism spectroscopy revealed only small changes in the
     secondary structures of D469 Delta and D361Y, demonstrating that the
     mutations do not dramatically affect the folding and stability of COMP.
     However, the local conformations of the type 3 repeats were disturbed, and
     the number of bound   ***calcium***   ions was reduced to 10 and 8,
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respectively. In addition to collagen I and II, collagen IX also binds to COMP with high affinity. The PSACH and MED mutations reduce the binding to collagens I, II, and IX and result in an altered zinc dependence. These interactions may contribute to the development of the patient phenotypes and may explain why MED can also be caused by mutations in collagen IX genes.

L9 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 2000464083 MEDLINE
DOCUMENT NUMBER: 20469946 PubMed ID: 11013461
TITLE: Delta 469 mutation in the type 3 repeat calcium binding domain of cartilage oligomeric matrix protein (COMP) disrupts calcium binding.
AUTHOR: Hou J; Putkey J A; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Houston Medical School, Houston, USA.
SOURCE: CELL CALCIUM, (2000 Jun) 27 (6) 309-14.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP/TSP5), a large glycoprotein found in the territorial matrix surrounding chondrocytes, is the fifth member of the thrombospondin (TSP) gene family. While the function of COMP is unknown, its importance is underscored by the finding that mutations in the highly conserved type 3 repeat domain causes two skeletal dysplasias. Pseudoachondroplasia (PSACH) and Multiple Epiphyseal Dysplasia, Fairbanks type (EDM1). The type 3 repeats are highly conserved low-affinity Ca(2+)binding domains that are found in all TSP genes. This study was undertaken to determine the effects of mutations on ***calcium*** binding and structure of the type 3 repeat domains. Wild-type (WT) and Delta469 ***recombinant*** COMP (rCOMP) proteins containing the entire ***calcium*** -binding domain were ***expressed*** in E. coli and purified. Equilibrium dialysis demonstrated that WT bound 10-12 Ca(2+)ions/molecule while Delta469 bound approximately half the Ca(2+)ions. Circular dichroism (CD) spectrometry had striking spectral changes for the WT in response to increasing concentrations of Ca(2+). These CD spectral changes were cooperative and reversible. In contrast, a large CD spectral change was not observed at any Ca(2+)concentration for Delta469. Moreover, both WT and Delta469 proteins produced similar CD spectral changes when titrated with Zn(2+), Cu(2+)and Ni(2+)indicating that the Delta469 mutation specifically affects only ***calcium*** binding. These results suggest that the Delta469 mutation, in the type 3 repeat region, interferes with Ca(2+)binding and that filling of all Ca(2+)binding loops may be critical for correct COMP protein conformation.

L9 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 2000458618 MEDLINE
DOCUMENT NUMBER: 20409010 PubMed ID: 10852928
TITLE: Cartilage oligomeric matrix protein is a calcium-binding protein, and a mutation in its type 3 repeats causes conformational changes.
AUTHOR: Chen H; Deere M; Hecht J T; Lawler J
CORPORATE SOURCE: Division of Tumor Biology and Angiogenesis, Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER: HL49081 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34) 26538-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009

ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925

AB Mutations in residues in the type 3 ***calcium*** -binding repeats and COOH-terminal globular region of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) lead to two skeletal dysplasias, pseudoachondroplasia and multiple epiphyseal dysplasia. It has been hypothesized that these mutations cause COMP to misfold and to be retained in the endoplasmic reticulum. However, this hypothesis is not supported by previous reports that COMP, when purified in the presence of EDTA, shows no obvious difference in electron microscopic appearance in the presence or absence of ***calcium*** ions. Since this discrepancy may be due to the removal of ***calcium*** during purification, we have ***expressed*** wild-type COMP and the most common mutant form found in pseudoachondroplasia, MUT3, using a mammalian ***expression*** system and have purified both proteins in the presence of ***calcium*** . Both proteins are ***expressed*** as pentamers. Direct ***calcium*** binding experiments demonstrate that wild-type COMP, when purified in the presence of ***calcium*** , is a ***calcium*** -binding protein. Rotary shadowing electron microscopy and limited trypsin digestion at various ***calcium*** concentrations show that there are conformational changes associated with ***calcium*** binding to COMP. Whereas COMP exists in a more compact conformation in the presence of ***calcium*** , it shows a more extended conformation when ***calcium*** is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less ***calcium*** and presents an intermediate conformation between the ***calcium*** -replete and ***calcium*** -depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of ***calcium*** binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

L9 ANSWER 4 OF 6 MEDLINE
ACCESSION NUMBER: 2000219197 MEDLINE
DOCUMENT NUMBER: 20219197 PubMed ID: 10753957
TITLE: A cartilage oligomeric matrix protein mutation associated with pseudoachondroplasia changes the structural and functional properties of the type 3 domain.
AUTHOR: Maddox B K; Mokashi A; Keene D R; Bachinger H P
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Oregon Health Sciences University, Portland, Oregon, 97201, USA.
CONTRACT NUMBER: AR45582 (NIAMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 14) 275 (15) 11412-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000505

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a member of the thrombospondin family of extracellular matrix glycoproteins. All members of the family contain a highly conserved region of thrombospondin type 3 sequence repeats that bind ***calcium*** . A mutation in COMP previously identified in a patient with pseudoachondroplasia resulted in abnormal sequestration of COMP in distinctive rER vesicles. The mutation, Asp-446 --> Asn, is located in the type 3 repeats of the molecule. This region was ***expressed*** in a mammalian culture with and without the mutation to study the structural or functional properties associated with the mutation. The biophysical parameters of the mutant peptide were compared with those of the wild type and revealed the following difference: secondary structural analysis by circular dichroism showed more alpha-helix content in the wild-type peptides. The ***calcium*** binding properties of the two peptides were significantly different; there were 17 ***calcium*** ions bound/wild-type COMP3 peptide compared with 8/mutant peptide. In addition, wild-type COMP3 had a higher affinity for ***calcium*** and bound

calcium more cooperatively. ***Calcium*** bound by the wild-type peptide was reflected in a structural change as indicated by velocity sedimentation. Thus, the effect of the COMP mutation appears to profoundly alter the ***calcium*** binding properties and may account for the difference observed in the structure of the type 3 domain. Furthermore, the highly cooperative binding of ***calcium*** to COMP3 suggests that these type 3 sequence repeats form a single protein domain, the thrombospondin type 3 domain.

L9 ANSWER 5 OF 6 MEDLINE
ACCESSION NUMBER: 1998420391 MEDLINE
DOCUMENT NUMBER: 98420391 PubMed ID: 9749943
TITLE: Characterization of cartilage oligomeric matrix protein (COMP) in human normal and pseudoachondroplasia musculoskeletal tissues.
AUTHOR: Hecht J T; Deere M; Putnam E; Cole W; Vertel B; Chen H; Lawler J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
CONTRACT NUMBER: HL 49081 (NHLBI)
SOURCE: MATRIX BIOLOGY, (1998 Aug) 17 (4) 269-78.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981124
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), the fifth member of the -thrombospondin gene family, is an extracellular matrix ***calcium*** -binding protein. The importance of COMP is underscored by the finding that mutations in COMP cause the human dwarfing condition, pseudoachondroplasia (PSACH). Here, we report the results of human tissue distribution and cell secretion studies of human COMP. COMP is ***expressed*** and secreted by cultured monolayer chondrocyte, tendon and ligament cells, and COMP secretion is not restricted to a differentiated chondrocyte phenotype. Whereas COMP is retained in the endoplasmic reticulum that accumulates within PSACH chondrocytes in vivo, COMP is not retained intracellularly in the dedifferentiated PSACH chondrocytes in cultures. These results lend further support to the hypothesis that retention of COMP is related to the terminal PSACH chondrocyte phenotype, processing of proteins related to extracellular matrix formation, and maintenance in cartilage.

L9 ANSWER 6 OF 6 MEDLINE
ACCESSION NUMBER: 93054522 MEDLINE
DOCUMENT NUMBER: 93054522 PubMed ID: 1429587
TITLE: COMP (cartilage oligomeric matrix protein) is structurally related to the thrombospondins.
AUTHOR: Oldberg A; Antonsson P; Lindblom K; Heinegard D
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Lund, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31) 22346-50.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D12746; GENBANK-D12747; GENBANK-D12748; GENBANK-D12749; GENBANK-D12750; GENBANK-D12751; GENBANK-D12752; GENBANK-D12753; GENBANK-X72914; GENBANK-Z14982
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19980206
Entered Medline: 19921201
AB Cloning and sequence analysis of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) cDNA, representing a cartilage pentameric protein, revealed a protein of 755 amino acid residues with a

calculated molecular mass of 82,700 Da. ***Expression*** of the cDNA in COS cells showed that COMP is a homopolymer composed of five identical disulfide-linked subunits. COMP is homologous to the carboxyl-terminal half of thrombospondin, and the homologies include 89% and 54% of the residues in COMP and thrombospondin, respectively. The similarities are most pronounced in the carboxyl-terminal domains and in the ***calcium*** binding type 3 repeat domains in which about 60% of the amino acid residues are identical. In the type 2/epidermal growth factor repeat domains the two proteins contain 41% identical residues. The sequence of the amino-terminal 84-amino acid residues is unique for COMP. Comparison of the amino acid sequences in the type 2 and type 3 repeat domains of COMP and the thrombospondins shows that COMP is the product of a unique gene and not the result of an alternatively spliced thrombospondin gene.

=> d his

(FILE 'HOME' ENTERED AT 09:57:26 ON 03 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 09:58:58 ON 03 JUL 2002

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L1          46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L2          12 S L1 (P) (RECOMBINANT OR EXPRESS?)
L3           5 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)
L4           0 S L3 (P) CALCIUM
L5         871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L6         256 S L5 (P) (RECOMBINANT OR EXPRESS?)
L7          28 S L6 (P) CALCIUM
L8           6 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
L9           6 S L8 NOT L3
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=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.83	43.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.24	-1.24

STN INTERNATIONAL LOGOFF AT 10:05:02 ON 03 JUL 2002

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FILE 'HOME' ENTERED AT 09:34:01 ON 03 JUL 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.42       0.42

FILE 'MEDLINE' ENTERED AT 09:35:12 ON 03 JUL 2002

FILE 'CAPLUS' ENTERED AT 09:35:12 ON 03 JUL 2002
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FILE 'AGRICOLA' ENTERED AT 09:35:12 ON 03 JUL 2002

=> s hcomp (a) protein
L1             0 HCOMP (A) PROTEIN

=> s (cartilage oligomeric matrix protein) or (thrombospondin-5)
   4 FILES SEARCHED...
L2           871 (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR (THROMBOSPONDIN-5)

=> s l2 (p) calcium
   2 FILES SEARCHED...
L3            68 L2 (P) CALCIUM

=> s human CARTILAGE OLIGOMERIC MATRIX PROTEIN
   3 FILES SEARCHED...
L4            46 HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN

=> s l4 not l3
L5            45 L4 NOT L3

=> s l5 (p) calcium
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L29 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L30 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L31 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L32 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L33 (P) CALCIUM'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L34 (P) CALCIUM'
L6             1 L5 (P) CALCIUM

=> d l6 1 ibib abs

L6   ANSWER 1 OF 1  EMBASE  COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   2001071433  EMBASE
TITLE:              Analysis of the promoter region of   ***human***
                      ***cartilage***     ***oligomeric***     ***matrix***
                      ***protein***   (COMP).
AUTHOR:             Deere M.; Rhoades Hall C.; Gunning K.B.; LeFebvre V.;
                    Ridall A.L.; Hecht J.T.
CORPORATE SOURCE:   J.T. Hecht, University of Texas, Medical School, Department
                    of Pediatrics, PO Box 20708, Houston, TX 77225-0708, United
                    States. Jacqueline.T.Hecht@uth.tmc.edu
```

SOURCE: Matrix Biology (2001) 19/8 (783-792).
Refs: 28
ISSN: 0945-053X CODEN: MTBOEC
PUBLISHER IDENT.: S 0945-053X(00)00127-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cartilage oligomeric matrix protein (COMP) is an extracellular matrix protein expressed in cartilage, ligament, and tendon. The importance of COMP in the matrix of these cells is underscored by the discovery that mutations in COMP cause the skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1). Here, we present the first report on the analysis of the human COMP promoter region in cartilage, ligament, and tendon cells. A 1.7-kb region of the COMP promoter has been cloned and sequenced and no TATA or CAAT boxes were found. Primer extension identified multiple transcription start sites. All four transcription start sites were utilized in chondrocytes with only three of them utilized in tendon and ligament cells. Differential regulation was observed for different parts of this 1.7-kb region with the 370-bp proximal region conveying the strongest promoter activity. The highest activity was observed in tendon and ligament. Finally, we provide evidence that the DNA binding protein SP1 plays a role in the regulation of COMP expression. These results indicate that COMP expression within these cells is regulated in a unique manner that differs from the expression of other extracellular matrix genes. Copyright .COPYRGT. 2001 Elsevier Science B.V./International Society of Matrix Biology.

=> d his

(FILE 'HOME' ENTERED AT 09:34:01 ON 03 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 09:35:12 ON 03 JUL 2002
L1 0 S HCOMP (A) PROTEIN
L2 871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR (THROMBOSPONDIN-5)
L3 68 S L2 (P) CALCIUM
L4 46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L5 45 S L4 NOT L3
L6 1 S L5 (P) CALCIUM

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L7 21 DUPLICATE REMOVE L3 (47 DUPLICATES REMOVED)

=> d l7 1-21 ibib abs

L7 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:248719 CAPLUS
DOCUMENT NUMBER: 136:399902
TITLE: Disease-causing mutations in cartilage oligomeric matrix protein cause an unstructured Ca2+ binding domain
AUTHOR(S): Kleerekoper, Quinn; Hecht, Jacqueline T.; Putkey, John A.
CORPORATE SOURCE: Departments of Biochemistry and Molecular Biology, Structural Biology Research Center, Houston Medical School, University of Texas, Houston, TX, 77030, USA
SOURCE: Journal of Biological Chemistry (2002), 277(12), 10581-10589
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chondrocytes from pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1) patients display an enlarged rough endoplasmic reticulum

that accumulates extracellular matrix proteins, including cartilage oligomeric matrix protein (COMP). Mutations that cause PSACH and EDM1 are restricted to a 27-kDa Ca2+ binding domain (type 3 repeat). This domain has 13 Ca2+-binding loops with a consensus sequence that conforms to Ca2+-binding loops found in EF hands. Most disease-causing mutations are found in the 11-kDa C-terminal region of this domain. The authors expressed recombinant native and mutant forms of the type 3 repeat domain (T3) and its 11-kDa C-terminal region (T3-Cterm). T3 and T3-Cterm bind .apprx.13 and 8 mol of Ca2+/mol of protein, resp. CD, one-dimensional proton, and two-dimensional 1H-15N HSQC spectra of Ca2+-bound T3-Cterm indicate a distinct conformation that has little helical secondary structure, despite the presence of 13 EF hand Ca2+-binding loops. This conformation is also formed within the context of the intact T3. 19 Cross-peaks found between 9.0 and 11.4 ppm are consistent with the presence of strong hydrogen bonding patterns, such as those in .beta.-sheets. Removal of Ca2+ leads to an apparent loss of structure as evidenced by decreased dispersion and loss of all down field resonances. Deletion of Asp-470 (a mutation found in 22% of all PSACH and EDM1 patients) decreased the Ca2+-binding capacity of both T3 and T3-Cterm by about 3 mol of Ca2+/mol of protein. Two-dimensional 1H-15N HSQC spectra of mutated T3-Cterm showed little evidence of defined structure in the presence or absence of Ca2+. The data demonstrate that Ca2+ is required to nucleate folding and to maintain defined structure. Mutation results in a partial loss of Ca2+-binding capacity and prevents Ca2+-dependent folding. Persistence of an unstructured state of the mutated Ca2+ binding domain in COMP is the structural basis for retention of COMP in the rough endoplasmic reticulum of differentiated PSACH and EDM1 chondrocytes.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:342407 BIOSIS
DOCUMENT NUMBER: PREV200200342407
TITLE: Disease-causing mutations in COMP cause an unstructured Ca2+ binding domain.
AUTHOR(S): Kleerekoper, Quinn (1); Hecht, Jacqueline T. (1); Putkey, John A. (1)
CORPORATE SOURCE: (1) Medical School, University of Texas-Houston, 6431 Fannin, Houston, TX, 77030 USA
SOURCE: Biophysical Journal, (January, 2002) Vol. 82, No. 1 Part 2, pp. 316a. http://intl.biophysj.org/. print.
Meeting Info.: 46th Annual Meeting of the Biophysical Society San Francisco, California, USA February 23-27, 2002
ISSN: 0006-3495.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 3 OF 21 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001698110 MEDLINE
DOCUMENT NUMBER: 21610998 PubMed ID: 11745002
TITLE: A novel mutation of the COMP gene in a Thai family with pseudoachondroplasia.
AUTHOR: Shotelersuk Vorasuk; Punyashthiti Rachaneekorn
CORPORATE SOURCE: Section on Medical Genetics and Metabolism, Department of Pediatrics, King Chulalongkorn Memorial Hospital, Bangkok 10330, Thailand.. vorasuk.s@chula.ac.th
SOURCE: INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, (2002 Jan) 9 (1) 81-4.
Journal code: 9810955. ISSN: 1107-3756.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20011218
Last Updated on STN: 20020308
Entered Medline: 20020307

AB Pseudoachondroplasia (PSACH) is an autosomal dominant disorder characterized by disproportionate short stature and precocious osteoarthritis. Radiographic manifestations include epiphyseal, metaphyseal and vertebral abnormalities. Mutations in the

(COMP) have been identified to cause PSACH. Most of them affect one of the eight ***calcium*** -binding domains of COMP. We describe a clinically and radiologically typical PSACH 4-year-old girl and her 31-year-old father. A novel mutation, 1345-1347CCC deletion in exon 13, of COMP was identified in both patients. The deletion would be expected to result in the loss of the conserved proline at codon 449 from the sixth ***calcium*** -binding domain. This result further supports that COMP is the only gene, discovered to date, responsible for PSACH across different populations and that the ***calcium*** -binding domains are important to the function of the normal COMP.

L7 ANSWER 4 OF 21 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001196441 MEDLINE
DOCUMENT NUMBER: 21125809 PubMed ID: 11084047
TITLE: Mutations in ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** causing pseudoachondroplasia and multiple epiphyseal dysplasia affect binding of ***calcium*** and collagen I, II, and IX.
AUTHOR: Thur J; Rosenberg K; Nitsche D P; Pihlajamaa T; Ala-Kokko L; Heinegard D; Paulsson M; Maurer P
CORPORATE SOURCE: Institute for Biochemistry, Medical Faculty, University of Cologne, D-50931 Koln, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Mar 2) 276 (9) 6083-92.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405
AB Mutations in type 3 repeats of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) cause two skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED). We expressed recombinant wild-type COMP that showed structural and functional properties identical to COMP isolated from cartilage. A fragment encompassing the eight type 3 repeats binds 14 ***calcium*** ions with moderate affinity and high cooperativity and presumably forms one large disulfide-bonded folding unit. A recombinant PSACH mutant COMP in which Asp-469 was deleted (D469 Delta) and a MED mutant COMP in which Asp-361 was substituted by Tyr (D361Y) were both secreted into the cell culture medium of human cells. Circular dichroism spectroscopy revealed only small changes in the secondary structures of D469 Delta and D361Y, demonstrating that the mutations do not dramatically affect the folding and stability of COMP. However, the local conformations of the type 3 repeats were disturbed, and the number of bound ***calcium*** ions was reduced to 10 and 8, respectively. In addition to collagen I and II, collagen IX also binds to COMP with high affinity. The PSACH and MED mutations reduce the binding to collagens I, II, and IX and result in an altered zinc dependence. These interactions may contribute to the development of the patient phenotypes and may explain why MED can also be caused by mutations in collagen IX genes.

L7 ANSWER 5 OF 21 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001640896 MEDLINE
DOCUMENT NUMBER: 21550102 PubMed ID: 11691584
TITLE: Selective intracellular retention of extracellular matrix proteins and chaperones associated with pseudoachondroplasia.
AUTHOR: Vranka J; Mokashi A; Keene D R; Tufa S; Corson G; Sussman M; Horton W A; Maddox K; Sakai L; Bachinger H P
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Portland, OR 97201, USA.
CONTRACT NUMBER: AR45582 (NIAMS)
SOURCE: MATRIX BIOLOGY, (2001 Nov) 20 (7) 439-50.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020205
Entered Medline: 20020204

AB Mutations in the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene result in pseudoachondroplasia (PSACH), which is a chondrodysplasia characterized by early-onset osteoarthritis and short stature. COMP is a secreted pentameric glycoprotein that belongs to the thrombospondin family of proteins. We have identified a novel missense mutation which substitutes a glycine for an aspartic acid residue in the thrombospondin (TSP) type 3 ***calcium*** -binding domain of COMP in a patient diagnosed with PSACH. Immunohistochemistry and immunoelectron microscopy both show abnormal retention of COMP within characteristically enlarged rER inclusions of PSACH chondrocytes, as well as retention of fibromodulin, decorin and types IX, XI and XII collagen. Aggrecan and types II and VI collagen were not retained intracellularly within the same cells. In addition to selective extracellular matrix components, the chaperones HSP47, protein disulfide isomerase (PDI) and calnexin were localized at elevated levels within the rER vesicles of PSACH chondrocytes, suggesting that they may play a role in the cellular retention of mutant COMP molecules. Whether the aberrant rER inclusions in PSACH chondrocytes are a direct consequence of chaperone-mediated retention of mutant COMP or are otherwise due to selective intracellular protein interactions, which may in turn lead to aggregation within the rER, is unclear. However, our data demonstrate that retention of mutant COMP molecules results in the selective retention of ECM molecules and molecular chaperones, indicating the existence of distinct secretory pathways or ER-sorting mechanisms for matrix molecules, a process mediated by their association with various molecular chaperones.

L7 ANSWER 6 OF 21 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2002026731 MEDLINE
DOCUMENT NUMBER: 21363816 PubMed ID: 11470401
TITLE: Calreticulin, PDI, Grp94 and BiP chaperone proteins are associated with retained COMP in pseudoachondroplasia chondrocytes.
AUTHOR: Hecht J T; Hayes E; Snuggs M; Decker G; Montufar-Solis D; Doege K; Mwalle F; Poole R; Stevens J; Duke P J
CORPORATE SOURCE: University of Texas Medical School at Houston, Department of Pediatrics, P.O. Box 20708, Houston, TX 77225-0708, USA.. jacqueline.t.hecht@uth.tmc.edu
SOURCE: MATRIX BIOLOGY, (2001 Jul) 20 (4) 251-62.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020131
Entered Medline: 20011207

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), a large pentameric glycoprotein and member of the thrombospondin (TSP) group of extracellular proteins, is found in the territorial matrix surrounding chondrocytes. More than 50 unique COMP mutations have been identified as causing two skeletal dysplasias: pseudoachondroplasia (PSACH); and multiple epiphyseal dysplasia (EDM1). Recent studies suggest that ***calcium*** -binding and ***calcium*** -induced protein folding differ between wild type and mutant proteins, and abnormal processing of the mutant COMP protein contributes to the characteristic enlarged lamellar appearing rER cisternae in PSACH and EDMI chondrocytes in vivo and in vitro. Towards the goal of delineating the pathogenesis of PSACH and EDM1, in-vivo PSACH growth plate and in-vitro PSACH chondrocytes cultured in alginate beads were examined to identify and localize the chaperone proteins participating in the processing of the retained extracellular matrix proteins in the PSACH rER. Aggrecan was localized to both the rER cisternae and matrix while COMP and type IX collagen were only found in the rER. Type II collagen was solely found in the ECM suggesting that it is processed and transported differently from other retained ECM proteins. Five chaperone proteins: BiP (Grp78); calreticulin (CRT); protein disulfide (PDI); ERp72; and Grp94, demonstrated

immunoreactivity in the enlarged PSACH cisternae and the shorter rER channels of chondrocytes from both in-vivo and in-vitro samples. The chaperone proteins cluster around the electron dense material within the enlarged rER cisternae. CRT, PDI and GRP94 AB-gold particles appear to be closely associated with COMP. Immunoprecipitation and Western blot, and Fluorescence Resonance Energy Transfer (FRET) analyses indicate that CRT, PDI and GRP94 are in close proximity to normal and mutant COMP and BiP to mutant COMP. These results suggest that these proteins play a role in the processing and transport of wild type COMP in normal chondrocytes and in the retention of mutant COMP in PSACH chondrocytes.

L7 ANSWER 7 OF 21 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000458618 MEDLINE
DOCUMENT NUMBER: 20409010 PubMed ID: 10852928
TITLE: ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** is a ***calcium*** -binding protein, and a mutation in its type 3 repeats causes conformational changes.
AUTHOR: Chen H; Deere M; Hecht J T; Lawler J
CORPORATE SOURCE: Division of Tumor Biology and Angiogenesis, Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER: HL49081 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34) 26538-44.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925
AB Mutations in residues in the type 3 ***calcium*** -binding repeats and COOH-terminal globular region of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) lead to two skeletal dysplasias, pseudoachondroplasia and multiple epiphyseal dysplasia. It has been hypothesized that these mutations cause COMP to misfold and to be retained in the endoplasmic reticulum. However, this hypothesis is not supported by previous reports that COMP, when purified in the presence of EDTA, shows no obvious difference in electron microscopic appearance in the presence or absence of ***calcium*** ions. Since this discrepancy may be due to the removal of ***calcium*** during purification, we have expressed wild-type COMP and the most common mutant form found in pseudoachondroplasia, MUT3, using a mammalian expression system and have purified both proteins in the presence of ***calcium*** . Both proteins are expressed as pentamers. Direct ***calcium*** binding experiments demonstrate that wild-type COMP, when purified in the presence of ***calcium*** , is a ***calcium*** -binding protein. Rotary shadowing electron microscopy and limited trypsin digestion at various ***calcium*** concentrations show that there are conformational changes associated with ***calcium*** binding to COMP. Whereas COMP exists in a more compact conformation in the presence of ***calcium*** , it shows a more extended conformation when ***calcium*** is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less ***calcium*** and presents an intermediate conformation between the ***calcium*** -replete and ***calcium*** -depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of ***calcium*** binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

L7 ANSWER 8 OF 21 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000219197 MEDLINE
DOCUMENT NUMBER: 20219197 PubMed ID: 10753957
TITLE: A cartilage oligomeric matrix protein mutation associated with pseudoachondroplasia changes the structural and functional properties of the type 3 domain.
AUTHOR: Maddox B K; Mokashi A; Keene D R; Bachinger H P
CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Oregon

Health Science University, Portland, Oregon, 97201, USA.
CONTRACT NUMBER: AR45582 (NIAM[redacted])
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 14) 275 (15) 11412-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000505

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a member of the thrombospondin family of extracellular matrix glycoproteins. All members of the family contain a highly conserved region of thrombospondin type 3 sequence repeats that bind ***calcium*** . A mutation in COMP previously identified in a patient with pseudoachondroplasia resulted in abnormal sequestration of COMP in distinctive rER vesicles. The mutation, Asp-446 --> Asn, is located in the type 3 repeats of the molecule. This region was expressed in a mammalian culture with and without the mutation to study the structural or functional properties associated with the mutation. The biophysical parameters of the mutant peptide were compared with those of the wild type and revealed the following difference: secondary structural analysis by circular dichroism showed more alpha-helix content in the wild-type peptides. The ***calcium*** binding properties of the two peptides were significantly different; there were 17 ***calcium*** ions bound/wild-type COMP3 peptide compared with 8/mutant peptide. In addition, wild-type COMP3 had a higher affinity for ***calcium*** and bound ***calcium*** more cooperatively. ***Calcium*** bound by the wild-type peptide was reflected in a structural change as indicted by velocity sedimentation. Thus, the effect of the COMP mutation appears to profoundly alter the ***calcium*** binding properties and may account for the difference observed in the structure of the type 3 domain. Furthermore, the highly cooperative binding of ***calcium*** to COMP3 suggests that these type 3 sequence repeats form a single protein domain, the thrombospondin type 3 domain.

L7 ANSWER 9 OF 21 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000464083 MEDLINE
DOCUMENT NUMBER: 20469946 PubMed ID: 11013461
TITLE: Delta 469 mutation in the type 3 repeat ***calcium*** binding domain of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) disrupts ***calcium*** binding.
AUTHOR: Hou J; Putkey J A; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Houston Medical School, Houston, USA.
SOURCE: CELL CALCIUM, (2000 Jun) 27 (6) 309-14.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP/TSP5), a large glycoprotein found in the territorial matrix surrounding chondrocytes, is the fifth member of the thrombospondin (TSP) gene family. While the function of COMP is unknown, its importance is underscored by the finding that mutations in the highly conserved type 3 repeat domain causes two skeletal dysplasias. Pseudoachondroplasia (PSACH) and Multiple Epiphyseal Dysplasia, Fairbanks type (EDM1). The type 3 repeats are highly conserved low-affinity Ca(2+)binding domains that are found in all TSP genes. This study was undertaken to determine the effects of mutations on ***calcium*** binding and structure of the type 3 repeat domains. Wild-type (WT) and Delta469 recombinant COMP (rCOMP) proteins containing the entire ***calcium*** -binding domain were expressed in E. coli and purified. Equilibrium dialysis demonstrated that

WT bound 10-12 Ca(2+)ions/molecule while Delta469 bound approximately half the Ca(2+)ions. Circular dichroism (CD) spectrometry had striking spectral changes for the WT in response to increasing concentrations of Ca(2+). These CD spectral changes were cooperative and reversible. In contrast, a large CD spectral change was not observed at any Ca(2+)concentration for Delta469. Moreover, both WT and Delta469 proteins produced similar CD spectral changes when titrated with Zn(2+), Cu(2+)and Ni(2+)indicating that the Delta469 mutation specifically affects only ***calcium*** binding. These results suggest that the Delta469 mutation, in the type 3 repeat region, interferes with Ca(2+)binding and that filling of all Ca(2+)binding loops may be critical for correct COMP protein conformation.

L7 ANSWER 10 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:400721 BIOSIS
DOCUMENT NUMBER: PREV199800400721
TITLE: Cartilage oligomeric matrix protein shows high affinity zinc-dependent interaction with triple helical collagen.
AUTHOR(S): Rosenberg, Krisztina; Olsson, Henric; Morgelin, Matthias; Heinegard, Dick (1)
CORPORATE SOURCE: (1) Lund Univ., Dep. Cell Molecular Biol., Section Connective Tissue Biol., P.O. Box 94, S-221 00 Lund Sweden
SOURCE: Journal of Biological Chemistry, (Aug. 7, 1998) Vol. 273, No. 32, pp. 20397-20403.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Cartilage and tendon extracellular matrices are composed of collagens, proteoglycans, and a number of noncollagenous proteins. Cartilage oligomeric matrix protein (COMP) is a prominent such protein, structurally related to the thrombospondins. We found that native COMP binds to collagen I/II and procollagen VII and that the interaction is dependent on the divalent cations Zn2+ or Ni2+, whereas Ca2+, Mg2+, and Mn2+ did not promote binding. Using a solid phase assay, Scatchard analysis identified one class of binding site with a dissociation constant (Kd) close to 1.5 nM in the presence of Zn2+. The results were confirmed by studies using surface plasmon resonance. Furthermore, metal chelate chromatography demonstrated that COMP bound Zn2+ and Ni2+. Electron microscopy showed that the interaction occurred at four defined sites on the 300-nm collagen and procollagen molecules. Two were located close to each end, and two at 126 and 206 nm, respectively, from the C-terminal. COMP interacted via its C-terminal globular domain and significantly only in the presence of Zn2+.

L7 ANSWER 11 OF 21 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1999120530 MEDLINE
DOCUMENT NUMBER: 99120530 PubMed ID: 9923655
TITLE: Retention of cartilage oligomeric matrix protein (COMP) and cell death in redifferentiated pseudoachondroplasia chondrocytes.
AUTHOR: Hecht J T; Montufar-Solis D; Decker G; Lawler J; Daniels K; Duke P J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
SOURCE: MATRIX BIOLOGY, (1998 Dec) 17 (8-9) 625-33.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 20020124
Entered Medline: 19990413
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a large extracellular glycoprotein that is found in the territorial matrix surrounding chondrocytes. Two skeletal dysplasias, pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (EDM1) are caused by mutations in the ***calcium*** binding domains of COMP. In this study, we identified two PSACH mutations and assessed the effect of these mutations on redifferentiated chondrocyte structure and function. We confirmed, in vitro, that COMP is retained in enormous cisternae of the rough endoplasmic reticulum (rER) and relatively absent in the PSACH

matrix. The rER accumulation may compromise chondrocyte function, leading to chondrocyte death. Moreover, while COMP appears to be deficient in the PSACH matrix, the matrix appeared to be normal but the over-all quantity was reduced. These results suggest that the abnormality in linear growth in PSACH may result from decreased chondrocyte numbers which would also affect the amount of matrix produced.

L7 ANSWER 12 OF 21 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1999094827 MEDLINE
DOCUMENT NUMBER: 99094827 PubMed ID: 9880218
TITLE: Identification of twelve mutations in cartilage oligomeric matrix protein (COMP) in patients with pseudoachondroplasia.
AUTHOR: Deere M; Sanford T; Ferguson H L; Daniels K; Hecht J T
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225-0708, USA.
CONTRACT NUMBER: CA16672 (NCI)
SOURCE: AMERICAN JOURNAL OF MEDICAL GENETICS, (1998 Dec 28) 80 (5) 510-3.
Journal code: 7708900. ISSN: 0148-7299.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990310
AB Pseudoachondroplasia (PSACH) is an autosomal dominant dwarfing condition characterized by disproportionate short stature, joint laxity, and early-onset osteoarthrosis. PSACH is caused by mutations in the gene encoding ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP). We are reporting on mutations in COMP in 12 patients with PSACH, including ten novel mutations. Eleven of the mutations are in exons 17A, 17B, and 18A, which encode the ***calcium*** -binding domains, and one mutation is in exon 19, which encodes part of the carboxy-terminal globular domain. Two of the mutations identified are the common delGAC(1430-1444) in exon 17B, which accounts for 36% of identified PSACH mutations. This report increases the range of mutations in COMP that cause PSACH and provides additional evidence for the importance of the ***calcium*** -binding domains and the globular domain to the function of COMP.

L7 ANSWER 13 OF 21 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998420391 MEDLINE
DOCUMENT NUMBER: 98420391 PubMed ID: 9749943
TITLE: Characterization of cartilage oligomeric matrix protein (COMP) in human normal and pseudoachondroplasia musculoskeletal tissues.
AUTHOR: Hecht J T; Deere M; Putnam E; Cole W; Vertel B; Chen H; Lawler J
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston, 77225, USA.
CONTRACT NUMBER: HL 49081 (NHLBI)
SOURCE: MATRIX BIOLOGY, (1998 Aug) 17 (4) 269-78.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981124
AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), the fifth member of the -thrombospondin gene family, is an extracellular matrix ***calcium*** -binding protein. The importance of COMP is underscored by the finding that mutations in COMP cause the human dwarfing condition, pseudoachondroplasia (PSACH). Here, we report the results of human tissue distribution and cell secretion studies of human COMP. COMP is expressed and secreted by cultured monolayer chondrocyte, tendon and ligament cells, and COMP secretion is not restricted to a

differentiated chondrocyte phenotype. Whereas COMP is retained in the endoplasmic reticulum that accumulates within PSACH chondrocytes in vivo, COMP is not retained intracellularly in the dedifferentiated PSACH chondrocytes in cultures. These results lend further support to the hypothesis that retention of COMP is related to the terminal PSACH chondrocyte phenotype, processing of proteins related to extracellular matrix formation, and maintenance in cartilage.

L7 ANSWER 14 OF 21 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97327574 MEDLINE
DOCUMENT NUMBER: 97327574 PubMed ID: 9184241
TITLE: Multiple epiphyseal dysplasia and pseudoachondroplasia due to novel mutations in the calmodulin-like repeats of cartilage oligomeric matrix protein.
AUTHOR: Susic S; McGrory J; Ahier J; Cole W G
CORPORATE SOURCE: Division of Orthopaedics, The Hospital for Sick Children and the University of Toronto, Ontario, Canada.
SOURCE: CLINICAL GENETICS, (1997 Apr) 51 (4) 219-24.
Journal code: 0253664. ISSN: 0009-9163.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19990129
Entered Medline: 19970723
AB A child with a mild form of pseudoachondroplasia was heterozygous for a deletion of 12 nucleotides from exon 10 of the ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) gene. It resulted in the deletion of valine 513 to lysine 516 from the eighth calmodulin-like repeat of COMP monomers. A child with the Fairbank's type of multiple epiphyseal dysplasia was also heterozygous for a COMP mutation. It substituted cysteine 371 by serine in the fourth calmodulin-like repeat. Both mutations were likely to alter the conformation and ***calcium*** binding of the mutant COMP protein chains. These findings support the proposal that deletions and insertions within the calmodulin-like domain produce pseudoachondroplasia, while amino acid substitutions with this domain may produce either pseudoachondroplasia or multiple epiphyseal dysplasia.

L7 ANSWER 15 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:110923 BIOSIS
DOCUMENT NUMBER: PREV199800110923
TITLE: Mutations in the Ca2+ binding domains of cartilage oligomeric matrix protein (COMP) cause decreased Ca2+ binding protein and conformational changes.
AUTHOR(S): Hou, J.; Putkey, J.; Hecht, J. T.
CORPORATE SOURCE: Univ. Texas Med. Sch. at Houston, Houston, TX USA
SOURCE: American Journal of Human Genetics, (Oct., 1997) Vol. 61, No. 4 SUPPL., pp. A174.
Meeting Info.: 47th Annual Meeting of the American Society of Human Genetics Baltimore, Maryland, USA October 28-November 1, 1997
ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:666081 CAPLUS
DOCUMENT NUMBER: 123:109410
TITLE: Pseudoachondroplasia and multiple epiphyseal dysplasia due to mutations in the cartilage oligomeric matrix protein gene
AUTHOR(S): Briggs, M. D.; Hoffman, S. M. G.; King, L. M.; Olsen, A. S.; Mohrenweiser, H.; Leroy, J. G.; Mortier, G. R.; Rimoin, D. L.; Lachman, R. S.; et al.
CORPORATE SOURCE: Dep. of Pediatrics, Cedars-Sinai Res. Inst., Los Angeles, CA, 90048, USA
SOURCE: Nat. Genet. (1995), 10(3), 330-6
CODEN: NGENEC; ISSN: 1061-4036
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pseudoachondroplasia (PSACH) d multiple epiphyseal dysplasi MED) are dominantly inherited chondrodysplasias characterized by short stature and early-onset osteo-arthrosis. The disease genes in families with PSACH and MED have been localized to an 800 kilobase interval on the short arm of chromosome 19. Recently the gene for cartilage oligomeric matrix protein (COMP) was localized to chromosome 19p13.1. In three patients with these diseases, we identified COMP mutations in a region of the gene that encodes a Ca++ binding motif. Our data demonstrate that PSACH and some forms of MED are allelic and suggest an essential role for Ca++ binding in COMP structure and function.

L7 ANSWER 17 OF 21 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 95400301 MEDLINE
DOCUMENT NUMBER: 95400301 PubMed ID: 7670471
TITLE: Mutations in exon 17B of cartilage oligomeric matrix protein (COMP) cause pseudoachondroplasia.
AUTHOR: Hecht J T; Nelson L D; Crowder E; Wang Y; Elder F F; Harrison W R; Francomano C A; Prange C K; Lennon G G; Deere M; +
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical School at Houston 77225, USA.
CONTRACT NUMBER: CA16672 (NCI)
HL49081 (NHLBI)
SOURCE: NATURE GENETICS, (1995 Jul) 10 (3) 325-9.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951026
Last Updated on STN: 19990129
Entered Medline: 19951018

AB Pseudoachondroplasia (PSACH) is a well characterized dwarfing condition mapping to chromosome 19p12-13.1. ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP), a cartilage specific protein, maps to the same location within a contig that spans the PSACH locus. Using single strand conformation polymorphism (SSCP) analysis and nucleotide sequencing we have identified COMP mutations in eight familial and isolated PSACH cases. All mutations involve either a single base-pair change or a three base-pair deletion in exon 17B. Six mutations delete or change a well conserved aspartic acid residue within the ***calcium*** -binding type 3 repeats. These results demonstrate that mutations in the COMP gene cause pseudochondroplasia.

L7 ANSWER 18 OF 21 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 95:711109 SCISEARCH
THE GENUINE ARTICLE: RW687
TITLE: PSEUDOACHONDROPLASIA AND MED RESULT FROM MUTATIONS IN THE ***CALCIUM*** -BINDING DOMAIN OF ***CARTILAGE*** ***OLIGOMERIC*** ***MATRIX*** ***PROTEIN*** (COMP)
AUTHOR: BRIGGS M D (Reprint); HOFFMAN S M G; KING L M; OLSEN A S; MOHRENWEISER H; LEROY J G; MORTIER G R; RIMOIN D L; GAINES E S; CEKLENIAK J A; KNOWLTON R G; COHN D H
CORPORATE SOURCE: CEDARS SINAI RES INST, LOS ANGELES, CA, 00000; CTR HUMAN GENOME, LIVERMORE, CA, 00000; GHENT MED SCH, GHENT, BELGIUM; THOMAS JEFFERSON UNIV, JEFFERSON MED COLL, PHILADELPHIA, PA, 19107
COUNTRY OF AUTHOR: USA; BELGIUM
SOURCE: AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 1995) Vol. 57, No. 4, Supp. S, pp. 241.
ISSN: 0002-9297.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L7 ANSWER 19 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:102777 BIOSIS
DOCUMENT NUMBER: PREV199698674912

TITLE: Distribution of CMP and COMP in human cartilage.
AUTHOR(S): Hauser, Nik ([illegible] Geiss, Jana; Niedhart, Michel[illegible]aulson, Mats (1); Hauselmann, Hans Jorg
CORPORATE SOURCE: (1) Inst. Biochem., Med. Fac., Univ. Cologne, Joseph-Stelzmann-Str. 52, D-50931 Cologne Germany
SOURCE: Acta Orthopaedica Scandinavica, (1995) Vol. 66, No. SUPPL. 266, pp. 72-73.
ISSN: 0001-6470.
DOCUMENT TYPE: Article
LANGUAGE: English

L7 ANSWER 20 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:476564 BIOSIS
DOCUMENT NUMBER: PREV199598490864
TITLE: Pseudoachondroplasia and MED result from mutations in the ***calcium*** binding domain of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP.
AUTHOR(S): Briggs, Michael D. (1); Hoffman, Susan M. G.; King, Lily M. (1); Olsen, Anne S.; Mohrenweiser, Harvey; Leroy, Jules G.; Mortier, Geert R.; Rimoin, David L. (1); Gaines, Erika S.; Cekleniak, Julia A.; Knowlton, Robert G.; Cohn, Daniel H. (1)
CORPORATE SOURCE: (1) Cedars-Sinai Res. Inst., Los Angeles, CA USA
SOURCE: American Journal of Human Genetics, (1995) Vol. 57, No. 4 SUPPL., pp. A47.
Meeting Info.: 45th Annual Meeting of the American Society of Human Genetics Minneapolis, Minnesota, USA October 24-28, 1995
ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 21 OF 21 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 93054522 MEDLINE
DOCUMENT NUMBER: 93054522 PubMed ID: 1429587
TITLE: COMP (cartilage oligomeric matrix protein) is structurally related to the thrombospondins.
AUTHOR: Oldberg A; Antonsson P; Lindblom K; Heinegard D
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Lund, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Nov 5) 267 (31) 22346-50.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D12746; GENBANK-D12747; GENBANK-D12748; GENBANK-D12749; GENBANK-D12750; GENBANK-D12751; GENBANK-D12752; GENBANK-D12753; GENBANK-X72914; GENBANK-Z14982
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19980206
Entered Medline: 19921201

AB Cloning and sequence analysis of ***cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) cDNA, representing a cartilage pentameric protein, revealed a protein of 755 amino acid residues with a calculated molecular mass of 82,700 Da. Expression of the cDNA in COS cells showed that COMP is a homopolymer composed of five identical disulfide-linked subunits. COMP is homologous to the carboxyl-terminal half of thrombospondin, and the homologies include 89% and 54% of the residues in COMP and thrombospondin, respectively. The similarities are most pronounced in the carboxyl-terminal domains and in the ***calcium*** binding type 3 repeat domains in which about 60% of the amino acid residues are identical. In the type 2/epidermal growth factor repeat domains the two proteins contain 41% identical residues. The sequence of the amino-terminal 84-amino acid residues is unique for COMP. Comparison of the amino acid sequences in the type 2 and type 3 repeat domains of COMP and the thrombospondins shows that COMP is the product of a unique gene and not the result of an alternatively spliced

thrombospondin gene.

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=> d his

     (FILE 'HOME' ENTERED AT 09:34:01 ON 03 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:35:12 ON 03 JUL 2002
L1             0 S HCOMP (A) PROTEIN
L2           871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR (THROMBOSPONDIN-5)
L3            68 S L2 (P) CALCIUM
L4            46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L5            45 S L4 NOT L3
L6             1 S L5 (P) CALCIUM
L7            21 DUPLICATE REMOVE L3 (47 DUPLICATES REMOVED)

=> s (biological matrix) or cartilage or (bone matrix) or collagen or hyaluronan or (fibrin gel) o
   4 FILES SEARCHED...
L8        596928 (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
                 OR HYALURONAN OR (FIBRIN GEL) OR (CARBON FIBER) OR (POLYLACTIC
                 ACID)

=> s l7 (p) l8
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L57 (P) L47'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L61 (P) L49'
L9            21 L7 (P) L8

=> s elisa kit
L10         3377 ELISA KIT

=> s l10 (p) (l2 or l4)
L11            0 L10 (P) (L2 OR L4)

=> s l7 (p) trypsin
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L84 (P) TRYPSIN'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L88 (P) TRYPSIN'
L12            1 L7 (P) TRYPSIN

=> s l12 not l7
L13            0 L12 NOT L7

=> d his

     (FILE 'HOME' ENTERED AT 09:34:01 ON 03 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     09:35:12 ON 03 JUL 2002
L1             0 S HCOMP (A) PROTEIN
L2           871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR (THROMBOSPONDIN-5)
L3            68 S L2 (P) CALCIUM
L4            46 S HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN
L5            45 S L4 NOT L3
L6             1 S L5 (P) CALCIUM
L7            21 DUPLICATE REMOVE L3 (47 DUPLICATES REMOVED)
L8        596928 S (BIOLOGICAL MATRIX) OR CARTILAGE OR (BONE MATRIX) OR COLLAGEN
L9            21 S L7 (P) L8
L10         3377 S ELISA KIT
L11            0 S L10 (P) (L2 OR L4)
L12            1 S L7 (P) TRYPSIN
L13            0 S L12 NOT L7

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FILE 'AGRICOLA' ENTERED AT 11:12:37 ON 03 JUL 2002

=> s (cartilage oligomeric matrix protein) or thrombospondin-5
   5 FILES SEARCHED...
L1          871 (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5

=> s l1 (p) trypsin
L2           15 L1 (P) TRYPSIN

=> duplicate remove l2
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L2
L3             3 DUPLICATE REMOVE L2 (12 DUPLICATES REMOVED)

=> d l3 1-3 ibib abs

L3   ANSWER 1 OF 3     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2000458618     MEDLINE
DOCUMENT NUMBER:    20409010   PubMed ID: 10852928
TITLE:              Cartilage oligomeric matrix protein is a calcium-binding
                    protein, and a mutation in its type 3 repeats causes
                    conformational changes.
AUTHOR:             Chen H; Deere M; Hecht J T; Lawler J
CORPORATE SOURCE:   Division of Tumor Biology and Angiogenesis, Department of
                    Pathology, Beth Israel Deaconess Medical Center and Harvard
                    Medical School, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER:    HL49081 (NHLBI)
SOURCE:             JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Aug 25) 275 (34)
                    26538-44.
                    Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200009
ENTRY DATE:         Entered STN: 20001005
                    Last Updated on STN: 20001005
                    Entered Medline: 20000925
AB   Mutations in residues in the type 3 calcium-binding repeats and
     COOH-terminal globular region of   ***cartilage***     ***oligomeric***
       ***matrix***     ***protein***   (COMP) lead to two skeletal dysplasias,
     pseudoachondroplasia and multiple epiphyseal dysplasia. It has been
     hypothesized that these mutations cause COMP to misfold and to be retained
     in the endoplasmic reticulum. However, this hypothesis is not supported by
     previous reports that COMP, when purified in the presence of EDTA, shows
     no obvious difference in electron microscopic appearance in the presence
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or absence of calcium ions. Since this discrepancy may be due to the removal of calcium during purification, we have expressed wild-type COMP and the most common mutant form found in pseudoachondroplasia, MUT3, using a mammalian expression system and have purified both proteins in the presence of calcium. Both proteins are expressed as pentamers. Direct calcium binding experiments demonstrate that wild-type COMP, when purified in the presence of calcium, is a calcium-binding protein. Rotary shadowing electron microscopy and limited ***trypsin*** digestion at various calcium concentrations show that there are conformational changes associated with calcium binding to COMP. Whereas COMP exists in a more compact conformation in the presence of calcium, it shows a more extended conformation when calcium is removed. MUT3, with a single aspartic acid deletion in the type 3 repeats, binds less calcium and presents an intermediate conformation between the calcium-replete and calcium-depleted forms of COMP. In conclusion, we show that a single mutation in the type 3 repeats of COMP causes the mutant protein to misfold. Our data demonstrate the importance of calcium binding to the structure of COMP and provide a plausible explanation for the observation that mutations in the type 3 repeats and COOH-terminal globular region lead to pseudoachondroplasia.

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998161946 MEDLINE
DOCUMENT NUMBER: 98161946 PubMed ID: 9501326
TITLE: The distribution of cartilage oligomeric matrix protein (COMP) in tendon and its variation with tendon site, age and load.
AUTHOR: Smith R K; Zunino L; Webbon P M; Heinegard D
CORPORATE SOURCE: Department of Farm Animal and Equine Medicine and Surgery, Royal Veterinary College, Hatfield, Hertfordshire, UK.
SOURCE: MATRIX BIOLOGY, (1997 Nov) 16 (5) 255-71.
Journal code: 9432592. ISSN: 0945-053X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980504

AB A protein prominent in guanidine hydrochloride extracts of adult bovine and equine digital flexor tendons was confirmed to be ***Cartilage*** ***Oligomeric*** ***Matrix*** ***Protein*** (COMP) by non-reducing and reducing SDS-PAGE, reaction with rabbit anti-COMP polyclonal antiserum on Western blots, ***trypsin*** digestion followed by HPLC on a C2/C18 column, and identification of COMP mRNA from tendon on Northern blots. Immunohistochemistry and Western blots of extracts showed COMP to be present in all regions of digital flexor tendons. Equine tendon COMP was purified by ion exchange chromatography and gel filtration and used in a heterologous inhibition ELISA to quantify COMP in equine digital flexor tendons at different ages, and in other tendons and ligaments. Mean COMP levels in digital flexor tendon were approximately 2-5mg/g wet weight, but they showed a large variation. Levels were low in neonatal tendon but rose rapidly during growth, with the metacarpal (tensional) superficial digital flexor tendon having the highest levels (approximately 10mg/g wet weight). Levels subsequently declined in this region, while in areas which experience a variable amount of compression, levels increased less but then remained constant. Extensor tendons and collateral ligaments, which experience less loading in vivo, had levels similar to those in neonatal tendon. COMP was identified in scarred skin and granulation tissue but not in normal skin, chronic fibrosis, or a fibrosarcomatous skin growth. A unilateral non-weight-bearing growing animal contained three to six times more COMP in the weight-bearing digital flexor tendons compared to the paralyzed limb, while the extensor tendons had similar amounts in both limbs. With the recent discovery of a COMP gene mutation causing pseudoachondroplasia (Hecht et al., 1995), in which lax tendons and ligaments are a feature, the present data suggest that COMP is synthesized in response to, and is necessary for tendon to resist, load.

L3 ANSWER 3 OF 3 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 97288369 MEDLINE
DOCUMENT NUMBER: 97288369 PubMed ID: 9143347

TITLE: Characterization of monoclonal antibodies recognizing different fragments of cartilage oligomeric matrix protein in human body fluids.

AUTHOR: Vilim V; Lenz M E; Vytasek R; Masuda K; Pavelka K; Kuettner K E; Thonar E J

CORPORATE SOURCE: Institute of Rheumatology, Praha, Czech Republic.. vilim@mbox.cesnet.cz

CONTRACT NUMBER: 1-P50-AR39239 (NIAMS)
AG04736 (NIA)

SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1997 May 1) 341 (1) 8-16.
Journal code: 0372430. ISSN: 0003-9861.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199706

ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19990129
Entered Medline: 19970603

AB ***Cartilage*** ***oligomeric*** ***matrix*** ***protein*** (COMP) is a high-molecular-weight glycoprotein found at a high concentration in articular cartilage. Recent studies have shown that the joint fluid and serum levels of antigenic COMP, measured by an enzyme-linked immunosorbent assay (ELISA) which uses a polyclonal antiserum raised against bovine COMP, provide important information about metabolic changes occurring in the cartilage matrix in joint disease. In this report, we describe the specificity of three monoclonal antibodies (mAbs) to human COMP and their usefulness in quantifying antigenic COMP fragments in body fluids. Two of the mAbs (16-F12 and 18-G3) recognized both oligomeric and monomeric forms of COMP, but the third (17-C10) reacted positively only with the former. Immunoblots of human COMP, predigested with ***trypsin*** for up to 6 h, showed that the three mAbs are directed against different epitopes identified on small tryptic fragments of 30 kDa (16-F12), 25 kDa (17-C10), and 40 kDa as well as 30 kDa (18-G3), respectively. The antibodies also recognized a different pattern of fragments in human pathological synovial fluids. This was particularly striking in the case of the medium size fragments (16-F12: 90 and 110 kDa; 17-C10: 70 and 90 kDa; 18-G3: up to five bands from 70 to 130 kDa). Competitive indirect inhibition ELISAs developed with mAbs 16-F12 and 17-C10 revealed further differences in the specificities of these antibodies. Thus, while mAb 16-F12 can be used only to quantify antigenic COMP in human synovial fluid and serum, mAb 17-C10 is useful in addition when analyzing canine and horse synovial fluid as well as canine serum. The results of analyses of synovial fluid samples from patients with osteoarthritis and rheumatoid arthritis provided preliminary evidence in support of the contention that measurement of the different COMP epitopes recognized by these mAbs in body fluids could prove useful in the clinical assessment of patients with joint disease.

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=> d his

     (FILE 'HOME' ENTERED AT 11:11:54 ON 03 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     11:12:37 ON 03 JUL 2002
L1          871 S (CARTILAGE OLIGOMERIC MATRIX PROTEIN) OR THROMBOSPONDIN-5
L2           15 S L1 (P) TRYPSIN
L3            3 DUPLICATE REMOVE L2 (12 DUPLICATES REMOVED)

=> lof y
LOF IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> log y
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
FULL ESTIMATED COST                           16.66      16.87
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